

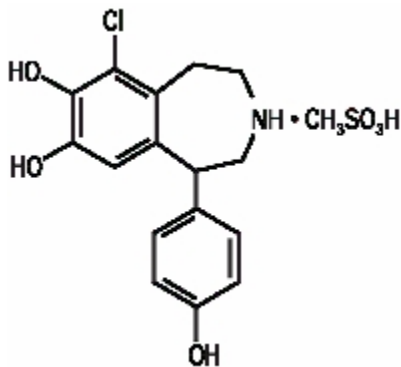
## FENOLDOPAM MESYLATE - fenoldopam mesylate injection

Bedford Laboratories

### Rx ONLY

#### DESCRIPTION

Fenoldopam Mesylate Injection USP is a dopamine D<sub>1</sub>-like receptor agonist. The product is formulated as a solution to be diluted for intravenous infusion. Chemically it is 6-chloro-2,3,4,5-tetrahydro-1-(*p*-hydroxy-phenyl)-1*H*-3-benzazepine-7,8-diol methanesulfonate (salt) with the following structure:



Fenoldopam mesylate is a white to off-white powder with a molecular weight of 401.87 and a molecular formula of C<sub>17</sub>H<sub>20</sub>ClNO<sub>6</sub>S.

It is sparingly soluble in water, ethanol and methanol, and is soluble in propylene glycol.

Each mL contains, in sterile aqueous solution, citric acid 3.44 mg; fenoldopam mesylate equivalent to fenoldopam 10 mg; propylene glycol 518 mg; sodium citrate dihydrate 0.61 mg; sodium metabisulfite 1 mg. The pH range is 2.8 to 3.8.

#### CLINICAL PHARMACOLOGY

##### Mechanism of Action

Fenoldopam is a rapid-acting vasodilator. It is an agonist for D<sub>1</sub>-like dopamine receptors and binds with moderate affinity to α<sub>2</sub>-adrenoceptors. It has no significant affinity for D<sub>2</sub>-like receptors, α<sub>1</sub> and β adrenoceptors, 5HT<sub>1</sub> and 5HT<sub>2</sub> receptors, or muscarinic receptors. Fenoldopam is a racemic mixture with the R-isomer responsible for the biological activity. The R-isomer has approximately 250-fold higher affinity for D<sub>1</sub>-like receptors than does the S-isomer. In non-clinical studies, fenoldopam had no agonist effect on presynaptic D<sub>2</sub>-like dopamine receptors, or α- or β-adrenoceptors, nor did it affect angiotensin-converting enzyme activity.

Fenoldopam may increase norepinephrine plasma concentration.

In animals, fenoldopam has vasodilating effects in coronary, renal, mesenteric and peripheral arteries. All vascular beds, however, do not respond uniformly to fenoldopam. Vasodilating effects have been demonstrated in renal efferent and afferent arterioles.

##### Pharmacokinetics

**Adult Patients:** Fenoldopam, administered as a constant infusion at dosages of 0.01 to 1.6 mcg/kg/min, produced steady-state plasma concentrations that were proportional to infusion rates. The elimination half-life was about 5 minutes in mild to moderate hypertensives, with little difference between the R (active) and S isomers. Steady state concentrations are attained in about 20 minutes (4 half-lives). The steady state plasma concentrations of fenoldopam, at comparable infusion rates, were similar in normotensive subjects and in patients with mild to moderate hypertension or hypertensive emergencies.

The pharmacokinetics of fenoldopam were not influenced by age, gender, or race in adult patients with a hypertensive emergency. There have been no formal drug-drug interaction studies using intravenous fenoldopam. Clearance of parent (active) fenoldopam is not altered in adult patients with end-stage renal disease on continuous ambulatory peritoneal dialysis (CAPD) and is not altered in adult patients with severe hepatic failure. The effects of hemodialysis on the pharmacokinetics of fenoldopam have not been evaluated.

**Pediatric Patients:** Information related to the pharmacokinetics of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

In radiolabeled studies in rats, no more than 0.005% of fenoldopam crossed the blood-brain barrier.

##### Excretion and Metabolism

Radiolabeled studies show that about 90% of infused fenoldopam is eliminated in urine, 10% in feces. Elimination is largely by conjugation, without participation of cytochrome P-450 enzymes. The principal routes of conjugation are methylation, glucuronidation, and sulfation. Only 4% of the administered dose is excreted unchanged. Animal data indicate that the metabolites are inactive.

## Pharmacodynamics and Clinical Studies

**Adult Patients:** In a randomized double-blind, placebo-controlled, 5-group study in 32 patients with mild to moderate essential hypertension (diastolic blood pressure between 95 and 119 mm Hg), and a mean baseline pressure of about 154/98 mm Hg, and heart rate of about 75 bpm, fixed-rate IV infusions of fenoldopam mesylate produced dose-related reductions in systolic and diastolic blood pressure. Infusions were maintained at a fixed rate for 48 hours. Table 1 shows the results of the study. The onset of response was rapid at all infusion rates, with the 15-minute response representing 50 to 100% of the one-hour response in all groups. There was some suggestion of partial tolerance at 48 hours in the two higher dose infusions, but a substantial effect persisted through 48 hours. When infusions were stopped, blood pressure gradually returned to pretreatment values with no evidence of rebound. This study suggests that there is no greater response to 0.8 mcg/kg/min than to 0.4 mcg/kg/min.

Table 1 PHARMACODYNAMIC EFFECTS OF FENOLDOPAM IN MILD TO MODERATE ADULT HYPERTENSIVE PATIENTS

Time Point and Mean Change From Time Zero ± SE	Drug Dosage (mcg/kg/min)				
	Placebo n=7	0.04 n=7	0.1 n=7	0.4 n=5	0.8 n=6
<b>15 Minutes of Infusion *</b>					
Systolic BP	0±6	-15±6	-19±8	-14±4	-24±6
Diastolic BP	0±2	-5±3	-12±4	-15±3	20±4
Heart rate	+2±2	+3±2	+5±1	+16±3	+19±3
<b>30 Minutes of Infusion *</b>					
Systolic BP	-6±5	-17±6	-18±6	-14±8	-26±6
Diastolic BP	-6±3	-7±3	-16±4	-14±3	-20±2
Heart rate	+2±2	+3±2	+10±2	+18±3	+23±3
<b>1 Hour of Infusion *</b>					
Systolic BP	-15±4	-22±7	-22±7	-26±9	-22±9
Diastolic BP	-5±3	-9±2	-18±4	-19±4	-21±1
Heart rate	+1±3	+5±2	+12±3	+19±4	+25±4
<b>4 Hours of Infusion *</b>					
Systolic BP	-14±5	-16±9	-31±15	-22±11	-25±7
Diastolic BP	-14±8	-8±4	-19±9	-25±3	-20±1
Heart rate	+5±3	+6±3	+10±4	+21±2	+27±7
<b>24 Hours of Infusion *</b>					
Systolic BP	-20±6	-23±8	-35±7	-22±6	-23±11
Diastolic BP	-11±6	-11±5	-23±10	-22±5	-13±3
Heart rate	+6±3	+5±3	+13±2	+17±4	+15±3
<b>48 Hours of Infusion *</b>					
Systolic BP	-12±8	-31±6	-22±8	-9±6	-14±10
Diastolic BP	-9±5	-10±6	-9±7	-9±2	-9±3
Heart rate	+1±2	0±4	+1±4	+12±3	+8±3

\*Mean change from time zero ± SE

In a multicenter, randomized, double-blind comparison of four infusion rates, fenoldopam mesylate was administered as constant rate infusions of 0.01, 0.03, 0.1 and 0.3 mcg/kg/min for up to 24 hours to 94 adult patients experiencing hypertensive emergencies (defined as diastolic blood pressure ≥120 mm Hg with evidence of compromise of end-organ function involving the cardiovascular, renal,

cerebral or retinal systems). Infusion rates could be doubled after one hour if clinically indicated. There were dose-related, rapid-onset, decreases in systolic and diastolic blood pressures and increases in heart rate (Table 2).

Table 2 PHARMACODYNAMIC EFFECTS OF FENOLDOPAM IN ADULT HYPERTENSIVE EMERGENCY PATIENTS

Time Point and Pharmacodynamic Parameters	Drug Dosage (mcg/kg/min)			
	0.01 n=25	0.03 n=24	0.1 n=22	0.3 n=23
<b>Pre-Infusion Baseline</b>				
Systolic BP- mean±SE	210±21	208±26	205±24	211±17
Diastolic BP- mean±SE	136±16	135±11	133±14	136±15
Heart rate- mean±SE	87±20	84±14	81±19	80±14
<b>15 Minutes of Infusion *</b>				
Systolic BP	-5±4	-7±4	-16±4	-19±4
Diastolic BP	-5±3	-8±3	-12±2	-21±2
Heart rate	-2±3	+1±1	+2±1	+11±2
<b>30 Minutes of Infusion *</b>				
Systolic BP	-6±4	-11±4	-21±3	-16±4
Diastolic BP	-10±3	-12±3	-17±3	-20±2
Heart rate	-2±3	-1±1	+3±2	+12±3
<b>1 Hour of Infusion * n</b>				
Systolic BP	-5±3	-9±4	-19±4	-22±4
Diastolic BP	-8±3	-13±3	-18±2	-23±2
Heart rate	-1±3	0±2	+3±2	+11±3
<b>4 Hours of Infusion * n</b>				
Systolic BP	-14±4	-20±5	-23±4	-37±4
Diastolic BP	-12±3	-18±3	-21±3	-29±3
Heart rate	-2±4	0±2	+4±2	+11±2

\*Mean change from baseline ± SE

Two hundred and thirty six severely hypertensive adult patients (DBP ≥120 mm Hg), with or without end-organ compromise, were randomized to receive in two open-label studies either fenoldopam or nitroprusside. The response rate was 79% (92/117) in the fenoldopam group and 77% (90/119) in the nitroprusside group. Response required a decline in supine diastolic blood pressure to less than 110 mm Hg if the baseline were between 120 and 150 mm Hg, inclusive, or by ≥40 mm Hg if the baseline were ≥150 mm Hg. Patients were titrated to the desired effect. For fenoldopam, the dose ranged from 0.1 to 1.5 mcg/kg/min; for nitroprusside, the dose ranged from 1.0 to 8.0 mcg/kg/min. As in the study in mild to moderate hypertensives, most of the effect seen at one hour is present at 15 minutes. The additional effect seen after 1 hour occurs in all groups and may not be drug-related (there was no placebo group for evaluation).

**Pediatric Patients:** Information related to the pharmacodynamics of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

## INDICATIONS AND USAGE

**Adult Patients:** Fenoldopam is indicated for the in-hospital, short-term (up to 48 hours) management of severe hypertension when rapid, but quickly reversible, emergency reduction of blood pressure is clinically indicated, including malignant hypertension with deteriorating end-organ function. Transition to oral therapy with another agent can begin at anytime after blood pressure is stable during fenoldopam mesylate infusion.

**Pediatric Patients:** Information related to the indicated use of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

## CONTRAINDICATIONS

None known.

## WARNINGS

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

## PRECAUTIONS

### Intraocular Pressure

In a clinical study of 12 patients with open-angle glaucoma or ocular hypertension (mean baseline intraocular pressure was 29.2 mm Hg with a range of 22 to 33 mm Hg), infusion of fenoldopam mesylate at escalating doses ranging from 0.05 to 0.5 mcg/kg/min over a 3.5 hour period caused a dose-dependent increase in intraocular pressure (IOP). At the peak effect, the intraocular pressure was raised by a mean of 6.5 mm Hg (range -2 to +8.5 mm Hg, corrected for placebo effect). Upon discontinuation of the fenoldopam mesylate infusion, the IOP returned to baseline values within 2 hours. Fenoldopam mesylate administration to patients with glaucoma or intraocular hypertension should be undertaken with caution.

### Tachycardia

Fenoldopam mesylate causes a dose-related tachycardia (Table 2), particularly with infusion rates above 0.1 mcg/kg/min. Tachycardia in adults diminishes over time but remains substantial at higher doses. Tachycardia in pediatric patients at doses  $\geq 0.8$  mcg/kg/min persists at least for 4 hours.

### Hypotension

Fenoldopam mesylate may occasionally produce symptomatic hypotension and close monitoring of blood pressure during administration is essential. (See ADVERSE REACTIONS.) It is particularly important to avoid systemic hypotension when administering the drug to patients who have sustained an acute cerebral infarction or hemorrhage. In pediatric patients, fenoldopam mesylate was only administered to patients with an indwelling intraarterial line.

### Hypokalemia

Decreases in serum potassium occasionally to values below 3 mEq/L were observed after less than 6 hours of fenoldopam infusion. It is not clear if the hypokalemia reflects a pressure natriuresis with enhanced potassium-sodium exchange or a direct drug effect. During clinical trials, electrolytes were monitored at intervals of 6 hours. Hypokalemia was treated with either oral or intravenous potassium supplementation. Patient management should include appropriate attention to serum electrolytes.

### Intracranial Pressure

The effect of fenoldopam in the presence of increased intracranial pressure has not been studied.

### Drug Interactions with Beta-Blockers

**Concomitant use of fenoldopam with beta-blockers should be avoided. If the drugs are used together, caution should be exercised because unexpected hypotension could result from beta-blocker inhibition of the sympathetic reflex response to fenoldopam.**

### Drug Interactions, General

Although there have been no formal interaction studies, intravenous fenoldopam mesylate has been administered safely with drugs such as digitalis and sublingual nitroglycerin. There is limited experience with concomitant antihypertensive agents such as alpha-blockers, calcium channel-blockers, ACE inhibitors, and diuretics (both thiazide-like and loop).

### Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 24-month study, mice treated orally with fenoldopam at 12.5, 25, or 50 mg/kg/day, reduced to 25 mg/kg/day on day 209 of study, showed no increase above controls in the incidence of neoplasms. Female mice in the highest dose group had an increased incidence and degree of severity of a fibro-osseous lesion of the sternum compared with control or low-dose animals. Compared to controls, female mice in the middle- and upper-dose groups had a higher incidence and degree of severity of chronic nephritis. These pathologic lesions were not seen in male mice treated with fenoldopam.

In a 24-month study, rats treated orally with fenoldopam at 5, 10 or 20 mg/kg/day, with the mid- and high-dose groups increased to 15 or 25 mg/kg/day, respectively, on day 372 of the study, showed no increase above controls in the incidence or type of neoplasms. Compared with the controls, rats in the mid- and high-dose groups had a higher incidence of hyperplasia of collecting duct epithelium at the tip of the renal papilla.

Fenoldopam did not induce bacterial gene mutation in the Ames test or mammalian gene mutation in the Chinese hamster ovary (CHO) cell assay. In the *in vitro* chromosomal aberration assay with CHO cells, fenoldopam was associated with statistically significant and dose-dependent increases in chromosomal aberrations, and in the proportion of aberrant metaphases. However, no chromosomal damage was seen in the *in vivo* mice micronucleus or bone marrow assays.

Oral fertility and general reproduction performance studies in male and female rats at 12.5, 37.5 or 75 mg/kg/day revealed no impairment of fertility or reproduction performance due to fenoldopam.

## Pregnancy

Teratogenic Effects; Pregnancy Category B.

Oral reproduction studies have been performed in rats and rabbits at doses of 12.5 to 200 mg/kg/day and 6.25 to 25 mg/kg/day, respectively. Studies have revealed maternal toxicity at the highest doses tested but no evidence of impaired fertility or harm to the fetus due to fenoldopam. However, there are no adequate and well-controlled studies in pregnant women. Since animal reproduction studies are not always predictive of human response, fenoldopam should be used in pregnancy only if clearly needed.

## Nursing Mothers

Fenoldopam is excreted in milk in rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when fenoldopam mesylate is administered to a nursing woman.

## Pediatric Use

Clinical study information related to the safety and effectiveness of fenoldopam injection in pediatric patients ages < 1 month to 12 years old is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

## Geriatric Use

Clinical studies of fenoldopam did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

## ADVERSE REACTIONS

**Adult Patients:** Fenoldopam mesylate causes a dose-related fall in blood pressure and increase in heart rate (see PRECAUTIONS; Tachycardia, and Hypotension). In controlled clinical studies of severe hypertension in patients with end-organ damage, 3% (4/137) of patients withdrew because of excessive falls in blood pressure. Increased heart rate could, in theory, lead to ischemic cardiac events or worsened heart failure, although these events have not been observed. The most common events reported as associated with fenoldopam mesylate use are headache, cutaneous dilation (flushing), nausea, and hypotension, each reported in more than 5% of patients.

### Adverse reactions in controlled trials in hypertensive adult patients

Adverse events occurring more than once in any dosing group (once if potentially important or plausibly drug-related) in the fixed-dose constant-infusion studies are presented in the following Table by infusion-rate group. There was no clear dose relationship, except possibly for headache, nausea, flushing.

Table 3 ADVERSE EVENTS\* FROM FIXED-DOSE INFUSION STUDIES BY DOSAGE GROUP

Body System	Fenoldopam Mesylate Dosage (mcg/kg/min) (Adults)						
	Event	Placebo (n=7)	0.01 (n=26)	0.03-0.04 (n=31)	0.1 (n=28)	0.3-0.4 (n=29)	0.6-0.8 (n=11)
Body, General	Headache	1	5	4	7	8	6
	Injection site reaction	0	1	3	0	3	2
Cardiovascular	ST-T abnormalities (primarily T-wave inversion)	0	2	4	0	1	0
	Flushing	0	0	0	0	1	3
	Hypotension <sup>†</sup>	0	0	0	2	0	2
	Postural hypotension	0	2	0	0	0	0
	Tachycardia <sup>†</sup>	0	0	0	0	0	2
Digestive	Nausea	0	3	0	3	5	4
	Vomiting	0	2	0	2	1	2
	Abdominal pain/fullness	0	2	0	0	2	1
	Constipation	0	0	0	0	0	2
	Diarrhea	0	0	0	0	2	0
Metabolic and Nutritional	Increased creatinine <sup>†</sup>	0	0	2	0	0	0

	Hypokalemia <sup>†</sup>	0	2	2	0	1	0
Nervous	Nervousness/anxiety	0	0	1	0	0	2
	Insomnia	0	2	0	0	0	0
	Dizziness	0	1	1	2	2	0
Respiratory	Nasal congestion	0	0	0	0	0	2
Skin and Appendages	Sweating	0	0	0	1	1	2
Urogenital	Urinary tract infection	0	2	0	1	0	0
Musculoskeletal	Back pain	0	1	0	1	2	2

\*Includes events reported by 2 or more patients receiving fenoldopam mesylate treatment across all dose groups.

<sup>†</sup>Investigator defined; no protocol definition.

### Adverse effects in overall database

The adverse event incidences listed below are based on observations of over 1,000 fenoldopam mesylate treated adult patients and not listed in the Table 3 above.

### Events reported with a frequency between 0.5 to 5% in patients treated with IV fenoldopam mesylate

<i>Cardiovascular:</i>	extrasystoles, palpitations, bradycardia, heart failure, ischemic heart disease, myocardial infarction, angina pectoris
<i>Metabolic:</i>	elevated BUN, elevated serum glucose, elevated transaminase, elevated LDH
<i>General Body:</i>	non-specific chest pain, pyrexia
<i>Hematologic/Lymphatic:</i>	leukocytosis, bleeding
<i>Respiratory:</i>	dyspnea, upper respiratory disorder
<i>Genitourinary:</i>	oliguria
<i>Musculoskeletal:</i>	limb cramp

**Pediatric Patients:** Information relating to treatment-emergent adverse events of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

### ANIMAL TOXICOLOGY

Unusual toxicologic findings (arterial lesions in the rat) with fenoldopam are summarized below. These findings have not been observed in mice or dogs. No evidence of a similar lesion in humans has been observed.

Arterial lesions characterized by medial necrosis and hemorrhage have been seen in renal and splanchnic arteries of rats given fenoldopam mesylate by continuous intravenous infusion at doses of 1 to 100 mcg/kg/min for 24 hours. The incidence of these lesions is dose related. Arterial lesions morphologically identical to those observed with fenoldopam have been reported in rats infused with dopamine. Data suggest that the mechanism for this injury involves activation of D<sub>1</sub>-like dopaminergic receptors. Such lesions have not been seen in dogs given doses up to 100 mcg/kg/min by continuous intravenous infusion for 24 hours, nor were they seen in dogs infused at the same dose for 6 hours daily for 24 days. The clinical significance of this finding is not known.

Oral administration of fenoldopam doses of 10 to 15 mg/kg/day or 20 to 25 mg/kg/day to rats for 24 months induced a higher incidence of polyarteritis nodosa compared to controls. Such lesions were not seen in rats given 5 mg/kg/day of fenoldopam or in mice given the drug at doses up to 50 mg/kg/day for 24 months.

### OVERDOSAGE

Intentional fenoldopam mesylate overdosage has not been reported. The most likely reaction would be excessive hypotension which should be treated with drug discontinuation and appropriate supportive measures.

### DOSAGE AND ADMINISTRATION

**Adult Patients:** The optimal magnitude and rate of blood pressure reduction in acutely hypertensive patients have not been rigorously determined, but, in general, both delay and too rapid decreases appear undesirable in sick patients. An initial fenoldopam mesylate injection dose may be chosen from Tables 1 and 2 in the CLINICAL PHARMACOLOGY section that produces the desired magnitude and rate of blood pressure reduction in a given clinical situation. Doses below 0.1 mcg/kg/min have very modest effects and appear only marginally useful in this population. In general, as the initial dose increases, there is a greater and more rapid blood pressure reduction. However, lower initial doses (0.03 to 0.1 mcg/kg/min) titrated slowly have been associated with less reflex tachycardia than have higher initial doses ( $\geq 0.3$  mcg/kg/min). In clinical trials, doses from 0.01 to 1.6 mcg/kg/min have been studied. Most of the effect of a given infusion rate is attained in 15 minutes.

Fenoldopam mesylate injection should be administered by continuous intravenous infusion. **A bolus dose should not be used.**

Hypotension and rapid decreases of blood pressure should be avoided. The initial dose should be titrated upward or downward, no

more frequently than every 15 minutes (and less frequently as goal pressure is approached) to achieve the desired therapeutic effect. The recommended increments for titration are 0.05 to 0.1 mcg/kg/min.

Use of a calibrated, mechanical infusion pump is recommended for proper control of infusion rate during fenoldopam mesylate injection infusion. In clinical trials, fenoldopam mesylate injection treatment was safely performed **without** the need for intra-arterial blood pressure monitoring; blood pressure and heart rate were monitored at frequent intervals, typically every 15 minutes. Frequent blood pressure monitoring is recommended.

Fenoldopam mesylate injection infusion can be abruptly discontinued or gradually tapered prior to discontinuation. Oral antihypertensive agents can be added during fenoldopam mesylate injection infusion or following its discontinuation. Patients in controlled clinical trials have received intravenous fenoldopam mesylate injection for as long as 48 hours.

## PREPARATION OF INFUSION SOLUTION

**WARNING: CONTENTS OF VIALS MUST BE DILUTED BEFORE INFUSION. EACH VIAL IS FOR SINGLE USE ONLY.**

### Dilution:

**Adult Patients:** The fenoldopam mesylate injection vial concentrate must be diluted in 0.9% Sodium Chloride Injection or 5% Dextrose Injection using the following dilution schedule:

mL of Concentrate (mg of drug)	Added to	Final Concentration
4 mL (40 mg)	1000 mL	40 mcg/mL
2 mL (20 mg)	500 mL	40 mcg/mL
1 mL (10 mg)	250 mL	40 mcg/mL

The drug dose rate must be individualized according to body weight and according to the desired rapidity and extent of pharmacodynamic effect. Table 4 provides the calculated infusion volume in mL/hour for a range of drug doses and body weights. The infusion should be administered using a calibrated mechanical infusion pump that can accurately and reliably deliver the desired infusion rate.

Infusion Rates:

Table 4 FENOLDOPAM ADULT INFUSION RATES (mL/hour) DRUG DOSAGE FOR ADULTS > 40 KG, USING 40 MCG/ML CONCENTRATION NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW: PEDIATRIC PATIENTS

Body Weight (kg)	Infusion Rate				
	0.025 mcg/kg/min	0.05 mcg/kg/min	0.1 mcg/kg/min	0.2 mcg/kg/min	0.3 mcg/kg/min
Infusion Rate (mL/hour) of 40 mcg/mL solution					
40	1.5	3	6	12	18
50	1.9	3.8	7.5	15	22.5
60	2.3	4.5	9.0	18	27
70	2.6	5.3	10.5	21	31.5
80	3	6	12	24	36
90	3.4	6.8	13.5	27	40.5
100	3.8	7.5	15	30	45
110	4.1	8.3	16.5	33	49.5
120	4.5	9	18	36	54
130	4.9	9.8	19.5	39	58.5
140	5.3	10.5	21	42	63
150	5.6	11.3	22.5	45	67.5

Table 4 (continued) FENOLDOPAM ADULT INFUSION RATES (mL/hour) DRUG DOSAGE FOR ADULTS > 40 KG, USING 40 MCG/ML CONCENTRATION NOTE: CONCENTRATION IS DIFFERENT FROM PEDIATRIC PATIENTS, SEE BELOW: PEDIATRIC PATIENTS

Body Weight (kg)	Infusion Rate					
	0.5 mcg/kg/min	0.8 mcg/kg/min	1 mcg/kg/min	1.2 mcg/kg/min	1.4 mcg/kg/min	1.6 mcg/kg/min
	Infusion Rate (mL/hour) of 40 mcg/mL solution					
40	30	48	60	72	84	96
50	37.5	60	75	90	105	120
60	45	72	90	108	126	144
70	52.5	84	105	126	147	168
80	60	96	120	144	168	192
90	67.5	108	135	162	189	216
100	75	120	150	180	210	240
110	82.5	132	165	198	231	264
120	90	144	180	216	252	288
130	97.5	156	195	234	273	312
140	105	168	210	252	294	336
150	112.5	180	225	270	315	360

The diluted solution is stable under normal ambient light and temperature conditions for at least 24 hours. Diluted solution that is not used within 24 hours of preparation should be discarded. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter or cloudiness is observed, the drug should be discarded.

**Pediatric Patients:** Information related to the dosing and administration of fenoldopam injection in pediatric patients is approved for Abbott Laboratories' fenoldopam drug products. However, due to Abbott's marketing exclusivity rights, this drug product is not labeled for pediatric use.

## HOW SUPPLIED

Fenoldopam Mesylate Injection USP is supplied in single-dose vials as follows:

**NDC 55390-071-01**, 10 mg/mL; 1 mL vial, individually boxed.

**NDC 55390-072-01**, 10 mg/mL; 2 mL vial, individually boxed.

Store at 2° to 30°C (35.6° to 86°F). Discard unused portion.

Manufactured by:

Ben Venue Laboratories, Inc.

Bedford, OH 44146

August 2004

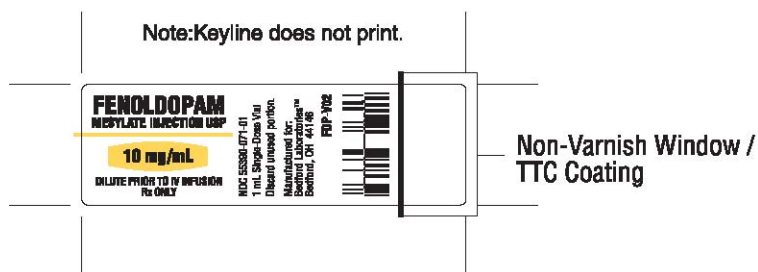
Manufactured for:

Bedford Laboratories™

Bedford, OH 44146

FDP-P01

## LABELS AND LABELING



Vial Label

Note: Keyline does not print.

**FENOLDOPAM**  
MESYLATE INJECTION USP  
**20 mg/2 mL**  
(10 mg/mL)  
DILUTE PRIOR TO IV INFUSION  
Rx ONLY

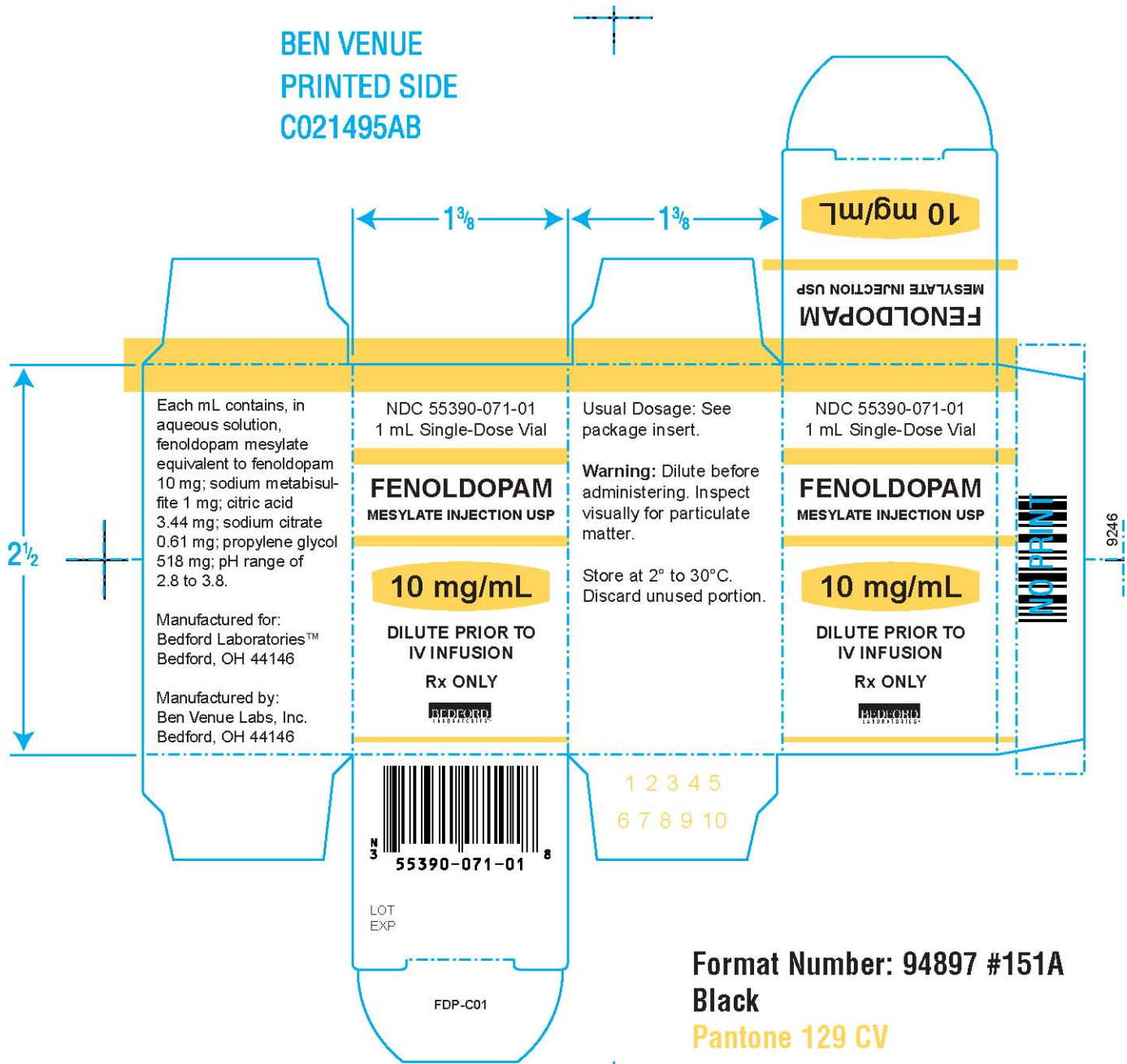
NDC 55390-071-01  
1 mL Single-Dose Vial  
Diluted/unadvised portion  
Manufactured for:  
Bedford Laboratories™  
Bedford, OH 44146  
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Non-Varnish Window /  
TTC Coating

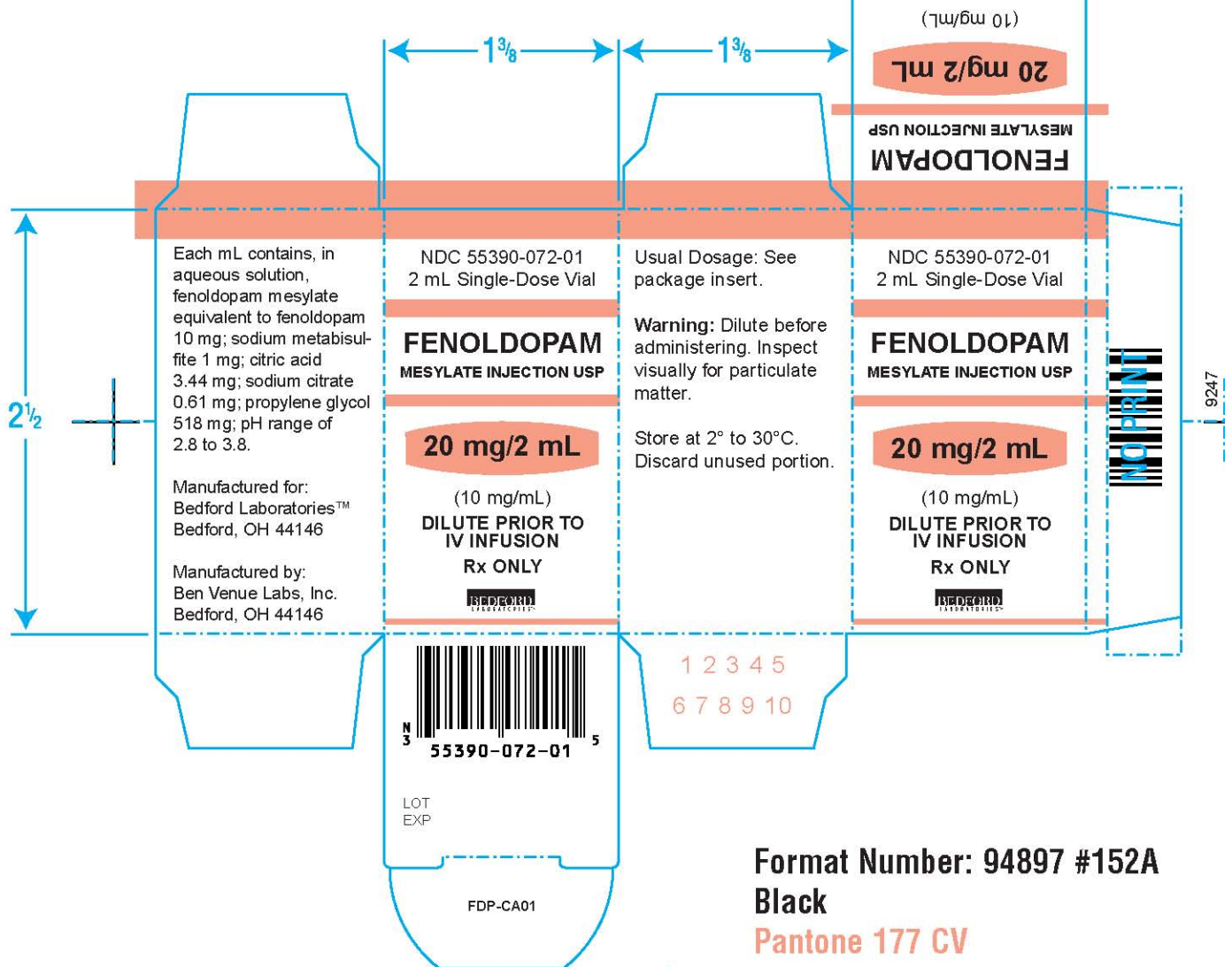
Vial Label

**BEN VENUE**  
**PRINTED SIDE**  
**C021495AB**



Unit Carton

BEN VENUE  
PRINTED SIDE  
C021495AB



Unit Carton